MUCOID SUBSTANCES AND CUTANEOUS CONNECTIVE TISSUE IN DERMATOSES

II. Mucoid Alterations in Degenerative and Congenital Dermatoses*

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A. The Mucoid Character of Basophilic Degeneration of Exposed and Senile Skin

The basophilic degeneration of the exposed and senile skin has been the subject of numerous investigations, ever since Unna (53), in 1894, described the basophilic masses as "Kollastin", a mixture of "Kollacin" and "Elacin" which, in turn, he regarded as degenerative products of collagen and elastin. Ferreira-Marques and van Uden (11), in 1950, discussed the controversy concerning the origin of the basophilic masses in detail. These authors quoted, among others, Kissmeyer and With (20), and Kreibich (23), in favor of their own contention of an essentially elastic nature of the degeneration. Ejiri (9), Dick (8) and Vernoni (54), after examining numerous specimens, came to the same conclusion, and Lever (28), in his textbook, also advocated this view. On the other hand, Percival et al. (41), maintained a collagenous character of the basophilic degeneration while Weidman (57), Hill and Montgomery (17), and others (10), tended to accept Unna's opinion of a mixed, collagenous-elastic nature of the masses.

More recently, in 1952, Tunbridge et al. (52) observed, with the electron microscope, a prevalence of collagen fibers in senile "elastosis".

In the past few years some histochemical investigations of exposed and senile skin were reported upon. Stoughton and Wells (50) observed with the periodic acid-Schiff ("PAS") stain after McManus (33) a ". . . definite increase of red-staining polysaccharides in the corium . . . especially of older subjects. . . . This change seemed to parallel the increase of acid orcein material" (Unna's "Kollastin"). Findlay (12) showed that the degenerating elastin in senile elastosis becomes increasingly PAS-fuchsinophilic, and that elastase abolishes the orceinophilia and PAS-fuchsinophilia of the degenerative masses. P. O'B. Montgomery (37) mentioned that "normal collagen and degenerated collagen both gave positive results with the periodic acid Schiff reaction" but he uses the term "degenerated collagen" for "collagen showing basophilic degeneration" without considering a possible basophilia of elastic tissue. Winer (59) described increase of elastic tissue, metachromasia with thionine, and fuchsinophilia with PAS of the basophilic masses, and he considered the involved tissue as modified collagen.

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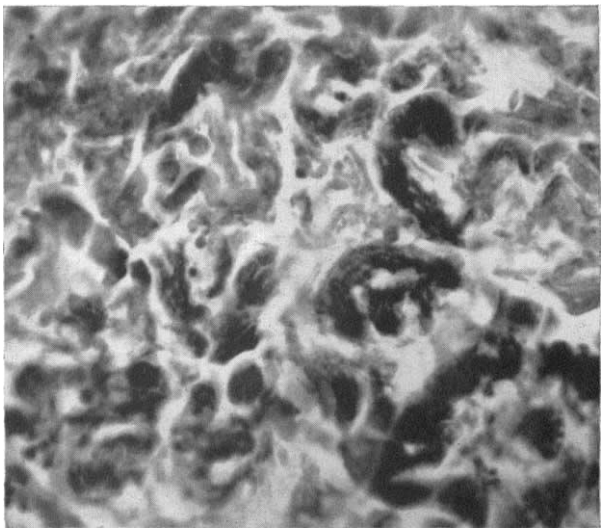

FIG. 1. Fiber conglomerate of basophilic degeneration. PAS stain. × 465. (Black-white picture × 585). The color ranges from orange-red to purple-red. No difference of fiber types.

Also quite recently, Gilman *et al.* (14), in a careful and detailed study, found the orceinophilic "elastotic" fibers of basophilic degeneration abnormal, both morphologically and tinctorially, especially with toluidine blue, although not readily distinguished from normal elastica with PAS or silver stains. Gilman and his co-workers considered the basophilic masses to be derived either from collagen or from faultily formed new fibers of all three types occurring in the cutis, i.e. of collagenous, elastic and reticulum fibers.

The first part of the present study attempts to clarify the controversial points and to define the nature of the basophilic degeneration by virtue of the distribution of PAS-fuchsinophilia and toluidine blue metachromasia in the different cutaneous fibers.

MATERIAL AND METHODS

Basophilic degeneration was studied in the exposed and/or senile skin of the following 56 lesions: 37 epitheliomas, 9 senile keratoses*, 3 seborrheic keratoses, 4 cutaneous horns, and 3 leukoplakias of the lips.

The histologic and histochemical methods used were the same as described in a previous study on connective tissue proliferation (48).

OBSERVATIONS

The basophilic connective tissue of exposed skin stains brilliant red with PAS. The coarsened, tortuous, lengthened or broken, and disorderly bundles are, depending on the degree of degeneration, purple, pink or orange (fig. 1). In milder cases only the superficial cutis is involved, and there is present a narrow, band-shaped zone of normal staining properties beneath the epidermis (see also

* A number of slides of senile keratoses were kindly provided by the Armed Forces Institute of Pathology, Washington 25, D. C.

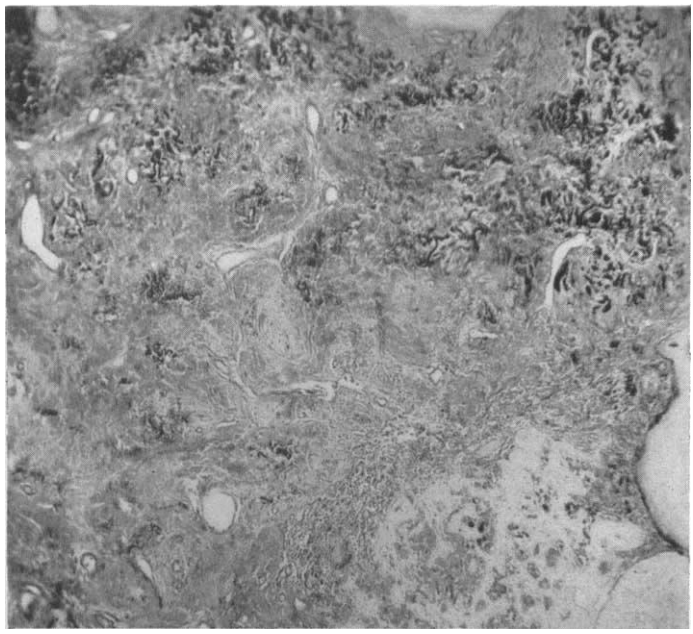

FIG. 2. Cutaneous basal cell epithelioma with extreme basophilic degeneration involving the entire cutis. PAS stain. × 60. The dark red-stained areas are PAS-positive, clumped fiber conglomerates; the light, almost unstained, yellow areas are epithelium, mainly epithelioma; the grayish, amorphous masses are pink-stained and represent the most advanced degeneration.

17, 28, 41, 57). In advanced stages, when the papillae have disappeared, the fuchsin-stained masses occupy also this subepidermal zone. In these cases the degeneration frequently penetrates deep into the cutis so that in extreme cases virtually the entire cutis is filled with degenerative tissue. With increasing severity and extent of the process the fibrous structure of the tissue becomes indistinct, and finally an amorphous mass of fibrinoid appearance replaces the cutis (fig. 2). At the same time, the PAS stain diminishes from red to pink, and only residual islands of degenerated bundles retain the red stain.

In sections stained for elastic tissue the extent of positive elastic staining corresponds well to the PAS-stained areas. The same tissue which is PAS-fuchsinophilic takes also the elastic stain. This parallelism of staining with PAS and resorcin-fuchsin or orcein applies also to the intensity of the staining. There is, however, one exception: In a few areas between the degenerated conglomerates there are sometimes irregular small collections of thin elastic fibers which remain unstained with PAS.

The mucopolysaccharide content of the orceinophilic masses is also demonstrable with toluidine blue (fig. 3). The clumped fibers and amorphous masses are metachromatic; however, they never show red, i.e. gamma metachromasia but only purple or pink, i.e. beta metachromasia. The papillary layer and the subepidermal zone are often diffusely pink or violet,—hence beta metachromatic.

After treatment with testicular hyaluronidase there is little change of the

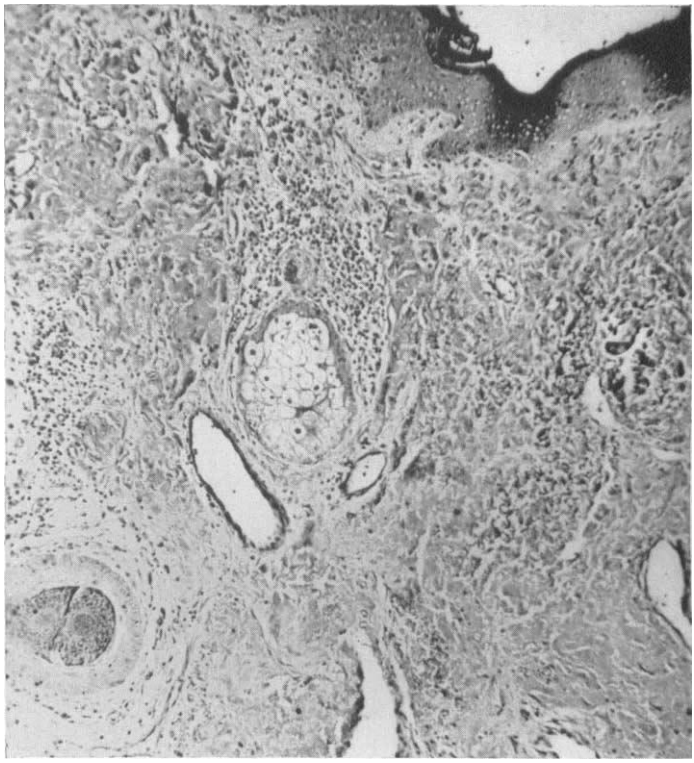

FIG. 3. Same specimen as in fig. 2. Toluidine blue stain. × 60. (Black-white picture × 90.) The darker, violet masses are conglomerates of basophilic degeneration, the lighter, amorphous masses show less pink-violet metachromasia. Epithelium (of epidermis and hair) dark, orthochromatic blue.

metachromasia or of fuchsin-staining with PAS. Strong metachromasis is somewhat reduced by hyaluronidase but the PAS stain and the beta metachromasia remain unaltered.

Silver-impregnated sections reveal a dense network of argyrophilic fibers in the degenerative conglomerates. These fibers are clearly abnormal. Often they are coarse, fragmented or shredded; and they do not always show a reticular pattern. Furthermore, in the advanced stages of degeneration the total amount of argyrophilic fibers is much reduced. The fibers frequently provide a marginal lining for coarse collagen bundles (see also (41)).

With PAS or toluidine blue the reticulum cannot be distinguished from other fibers, and, similarly, collagen and elastic fibers cannot be distinguished from each other (see also (14)). In superficial conglomerates there are no elastic fibers visible, and where the degeneration penetrates more deeply into the cutis, there too, no normal elastic tissue can be recognized. In the amorphous masses of advanced degeneration there is, except for a residual atrophic reticulum, no fibrous structure at all. The PAS and toluidine blue stains therefore reveal that

all three cutaneous fiber types are morphologically and tinctorially abnormal in exposure-damaged skin.

COMMENTS

With the methods employed great amounts of mucopolysaccharides and mucoproteins are demonstrable in the exposure-damaged cutaneous tissue. These mucopolysaccharides cover the fiber bundles and bundle conglomerates of the degenerated tissue. The amount of these mucopolysaccharides is not the same at all stages of degeneration; the PAS stain and the toluidine blue metachromasia diminish in advanced degeneration.

Beta metachromasia and hyaluronidase-fastness characterize the great bulk of the mucoid substances as mucoproteins (35, 40, 58); wherever fiber conglomerates show diminution of PAS staining and metachromasia after hyaluronidase the presence of free acid mucopolysaccharides can also be assumed (35, 40, 58).

All these mucopolysaccharides and mucoproteins are constitutents of the ground substance; the fiber conglomerates of the basophilic tissue contain, therefore, an admixture of ground substance. The diminution of this admixture in the amorphous masses is, however, unexplained. Although these masses show a fibrinoid appearance, yet they cannot be interpreted as fibrinoid; their derivation from merged fibers and matrix substance, their orceinophilia and partial argyrophilia are all in accord with properties of fibrinoid (5, 14, 40); however, they are not eosinophilic like fibrinoid (5, 40), and Gilman et al. (14) state explicitly that the basophilic masses do not contain fibrinoid because they stain pale yellow or not at all with phosphotungstic acid hematoxylin while fibrinoid stains purple with this dye.

Numerous argyrophilic fibers pervade the basophilic conglomerates (see also (41)). They represent an attempt at regeneration of collagen as is particularly obvious from those reticulum fibers which form a lining of collagen bundles; this relationship between collagen and reticulum is characteristic for developing fibrous tissues (14, 41, 44, 46, 48, 56). Reticulum is PAS-positive (29, 30, 31, 33, 44, 48) and therefore cannot be distinguished from the other fuchsinophilic fibers of the basophilic conglomerates in PAS stains.

Despite the presence of the argyrophilic fibers there is no new formation of collagen in exposure-damaged skin. This can perhaps be explained by the abnormal character of the argyrophilic fibers. Regression and morphologic degeneration of reticulum were previously described (38, 41, 56); also, a tinctorially abnormal reticulum occurs in the stroma of many cutaneous tumors and granulomas (48). The advanced atrophy of the reticulum in the amorphous masses is perhaps comparable to the regression described by Morrione (38).

Unlike PAS, the silver stain always identifies reticulum fibers, normal or abnormal. By contrast, neither PAS nor toluidine blue or any other of the used stains identifies collagenous or elastic fibers in the areas of basophilic degeneration. Nevertheless, certain morphologic and tinctorial characteristics of the fiber conglomerates permit some identification of the fibers' nature.

The orceinophilia of the fiber conglomerates does not prove their elastic nature;

the sheer mass of the degeneration speaks against this interpretation (32). On the other hand, it is quite possible, and even likely, that originally elastic tissue constitutes a certain portion of the conglomerates. However, this tissue must be abnormal because it does not show the morphology of normal elastica (see also (14)) and it differs also tinctorially from normal elastic tissue. The elastica of loose connective tissue ordinarily is not at all, or only weakly, PAS-positive (24, 25); but under abnormal conditions, e.g. if it is over-oxydized, it can become PAS-positive (12, 14, 24, 25). This type of fibers may, for instance, be present in the stroma of nevi, melanomas and leukemia (48). PAS-fuchsinophilia therefore is consistent with the presence of abnormal elastic fibers. The strongest argument, however, for the presence of elastic tissue in the fiber conglomerates is Findlay's observation (12), that elastase abolishes the PAS-fuchsinophilia of the masses.

On the other hand, the electron-microscopic findings of Tunbridge, et al. (43, 52, see above) and the observations of Percival and his co-workers (41) prove the presence of collagen in the basophilic conglomerates. The positive reaction of these fibers to PAS is consistent with their collagenous nature; abnormal collagenous fibers coated with ground substance are quite common in pathological tissues (48). They are of regular occurrence and definitely far more common than PAS-positive elastica. Histochemically, therefore, the collagenous nature of the bulk of the degenerative fibers is more likely than their origin from elastica. Certainly, the contention of purely elastic fiber conglomerates (8, 9, 20, 23, 33, 54) cannot be maintained.

Basophilic degeneration is therefore a conglomeration of abnormal ("faultily formed" (7)) collagenous, elastic and argyrophilic fibers with great amounts of mucopolysaccharides of the ground substance.

B. Mucoid Changes in Degenerative Diseases and Congenital Dysplasias of the Skin

Despite the continuing interest in "collagen diseases" little has been reported, in recent years, upon the histochemistry of the skin lesions in these diseases. Stoughton and Wells (50), using the periodic acid-Schiff-McManus stain ("PAS"), described increases in PAS-positive substances, (i.e. mucopolysaccharides), in vascular walls, epidermal basal membrane and subepidermal corium of lupus erythematosus. None of these changes were seen by the authors in scleroderma. Asboe-Hansen (3) demonstrated by means of the toluidine blue metachromasia a considerable increase of hyaluronic acid, diffusely, in irregular strands, and in masses, in the cutis of lupus erythematosus. In scleroderma there was also moderate, partly hyaluronidase-labile metachromasia. Likewise, Watrin (55), Meneghini and Pozzo (34), and Leoni and Rossetti (27) observed metachromasia and increase in PAS-positive substances in the cutis of lupus erythematosus. Mucoid changes in scleroderma were also described (27). Winer (59) noticed abnormal PAS staining in scleroderma (morphea) which he atrributed to elastomucin. Braun-Falco (6) described increase of a PAS-positive, non-metachromatic substance in the thickened epidermal basement membrane, in the vascular walls, and in the upper corium of chronic lupus erythematosus. He ascribed most of the

mucoid changes to the PAS-positive argyrophilic fibers which were morphologically of abnormal appearance. Grupper and Plas (16) observed PAS-positive fiber bundles in the degenerative tissue of granuloma annulare.

Findlay (12) found the elastase-resistant elastic tissue of pseudoxanthoma elasticum only slightly PAS-fuchsinophilic. He, as well as Winer, pointed out (59) that elastic tissue becomes fuchsinophilic only if elastomucin is released by a breakdown of fibers. Katz and Steiner (19) observed a diffuse increase of PAS-positive, metachromatic substance in the papillary bodies and at the dermo-epidermal junction in lesions of Ehlers-Danlos' syndrome.

The following part of the study describes the mucoid changes of the cutaneous connective tissue in degenerative skin diseases and congenital dysplasias as demonstrated by the PAS and toluidine stains, and it correlates the observed changes with certain alterations of the cutaneous connective tissue fibers.

The type and number of lesions which were examined in this part of the study are shown in Table 1. The histologic and histochemical methods used were the same as described in Part A.

OBSERVATIONS

In the upper cutis of chronic radiodermatitis and of many cases of chronic lupus erythematosus there are conglomerates of PAS-positive fiber bundles which stain brilliantly red, purple or pink. These masses represent the basophilic degeneration of the connective tissue in the exposed skin (cf. Part A).

The basal membranes in lupus erythematosus, scleroderma, scleredema and chronic radiodermatitis are conspicuously PAS-positive, red or pink, and more or less thickened (fig. 4). Also, a rich network of argyrophilic fibers is outlined in red in the PAS-stained sections of chronic radiodermatitis, granuloma annulare and connective tissue nevus (fig. 5). In Ehler-Danlos' syndrome (19), and in scleroderma and scleredema residual papillae and a thin subepidermal band show a diffuse pink stain which diminishes gradually downwards. There is also some orange-brown streaking and spotting of fiber bundles in the deep corium of scleroderma, scleredema and pseudoxanthoma elasticum.

With toluidine blue the PAS-positive basophilic fiber conglomerates of chronic radiodermatitis and lupus erythematosus are beta metachromatic, violet or pink (see 3, 59 and Part A). The numerous reticulum fibers of radiodermatitis and granuloma annulare are also beta metachromatic. The subepidermal zone and the papillae of scleroderma, scleredema and Ehler-Danlos' syndrome (19) are characterized by a pink or violet color (fig. 6). The elastic curls of pseudoxanthoma elasticum are orthochromatic, i. e. blue (fig. 7). Orthochromasia is also present in chronic lymphedema. The intensely PAS-positive basal membranes of lupus erythematosus, scleroderma, scleredema and chronic radiodermatitis show no distinct metachromasia or only a weak beta staining.

Testicular hyaluronidase effects either no change of the toluidine blue stain or an indefinite diminution of the beta metachromasia.

In silver-impregnated sections the amount and extent of the argyrophilic fibers of chronic radiodermatitis, granuloma annulare and connective tissue

TABLE 1

Degenerative diseases and congenital dysplasias

Diagnosis	PAS Staining		Toluidine Blue Metachromasia		Reticulum	Elastica
	Increased in basal membranes and vascular walls	Of papillae and subepidermal zones	Hyaluronidase-stable, beta metachromatic	Orthochromatic		
Lupus erythematosus (10 chronic discoid, 2 subacute disseminated)	+		b.m., v.w.* weak		reduced, degenerated	reduced
Scleroderma (7)	+	+	b.m., v.w.* weak; p. s.z.† distinct		reduced, degenerated	reduced
Sclerodema adultorum (1)	+	+	b.m., v.w.* weak; p. and s.z.† distinct		reduced, degenerated	reduced
Chronic radio-dermatitis (1)	+		b.m., v.w.* weak		increased, normal	atrophic
Granuloma annulare (2)			weak		increased, normal	almost atrophic
Chronic lymphedema (1)				+	absent	normal
Pseudoxanthoma elasticum (2)				+	reduced, degenerated	increased, curled
Ehlers-Danlos' syndrome (2)		+	distinct		papillary increase	normal
Connective tissue nevus (1)					? degenerative	reduced

* b.m. = basal membranes; v.w. = vascular wall.

† p. and s.z. = papillary and subepidermal zone.

Slides from one case each of pseudoxanthoma elasticum and Ehlers-Danlos' syndrome were kindly provided by the Armed Forces Institute of Pathology, Washington 25, D. C., and slides from a connective tissue nevus were kindly supplied by the New York Skin and Cancer Unit, New York, N. Y. (Dr. M. B. Sulzberger).

nevus corresponds to the rich reticulum of these lesions demonstrated with PAS and toluidine blue. In the connective tissue nevus the argyrophilic fibers are unusually coarse, straight and long, or fragmented and apparently nowhere near blood vessels (fig. 8). By contrast, the argyrophilic fibers in the subepidermal zone and in the infiltrate of lupus erythematosus are often thin, fragmented, rod-like, and without reticular arrangement. Similarly, in scleroderma and scleredema only fine argyrophilic shreds remain in the residual papillae, subepidermal and in the basal membrane (fig. 9). The reticulum is also considerably reduced in pseudoxanthoma elasticum and completely absent in chronic lymphedema. On the other hand, the papillary bodies of Ehlers-Danlos' syndrome show a moderate increase in argyrophilic fibers.

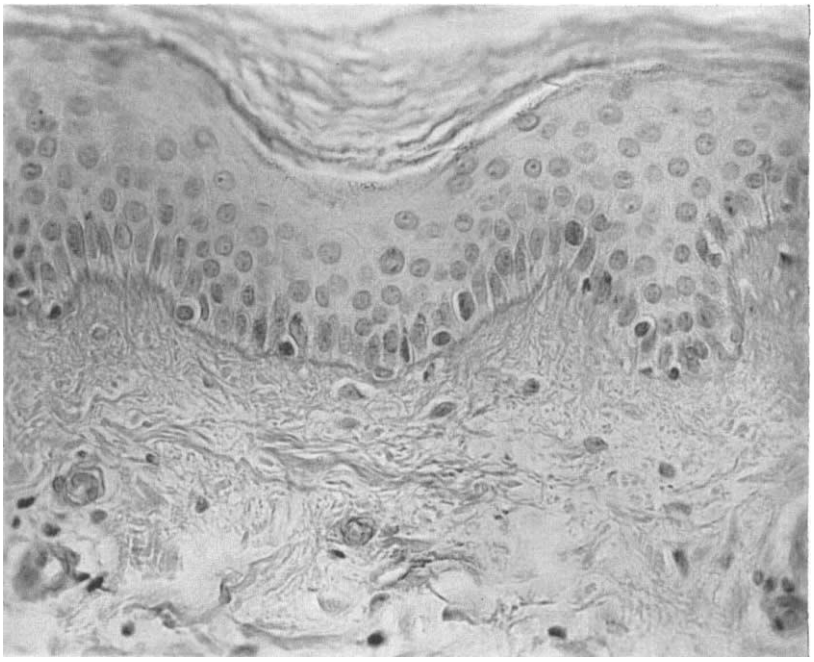

FIG. 4. Generalized scleroderma. PAS stain. × 360. Increased staining of basal membrane and vascular walls. Slight diffuseness of subepidermal zone.

FIG. 5. Connective tissue nevus. PAS stain. × 265. Long, rather straight, and short, thick, dark red stained fibers and swelling of collagen bundles. Compare with fig. 8.

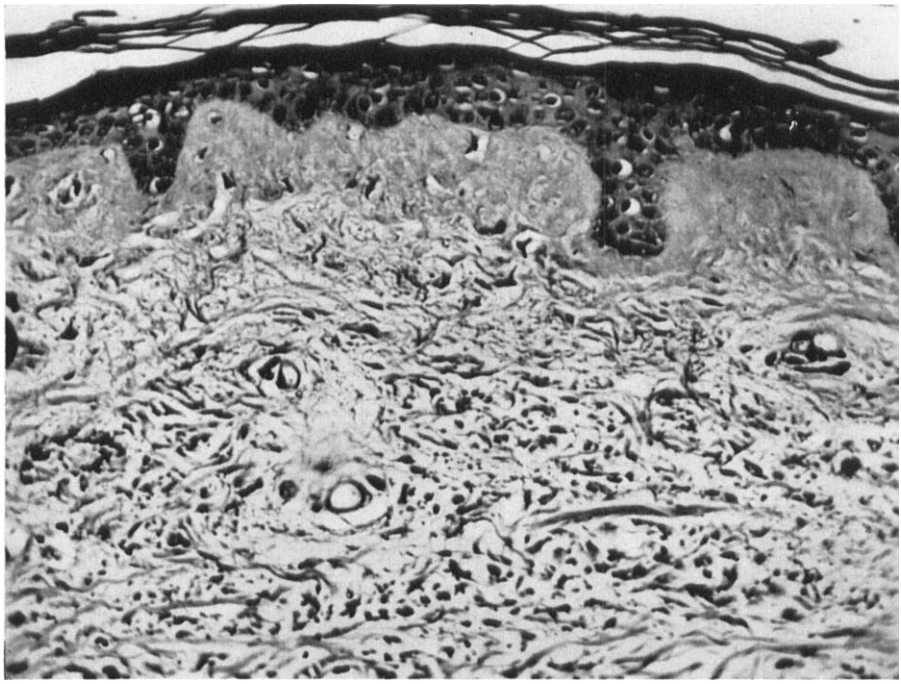

FIG. 6. Generalized scleroderma. Toluidine blue stain. × 260. Distinct beta metachromasia of subepidermal zone.

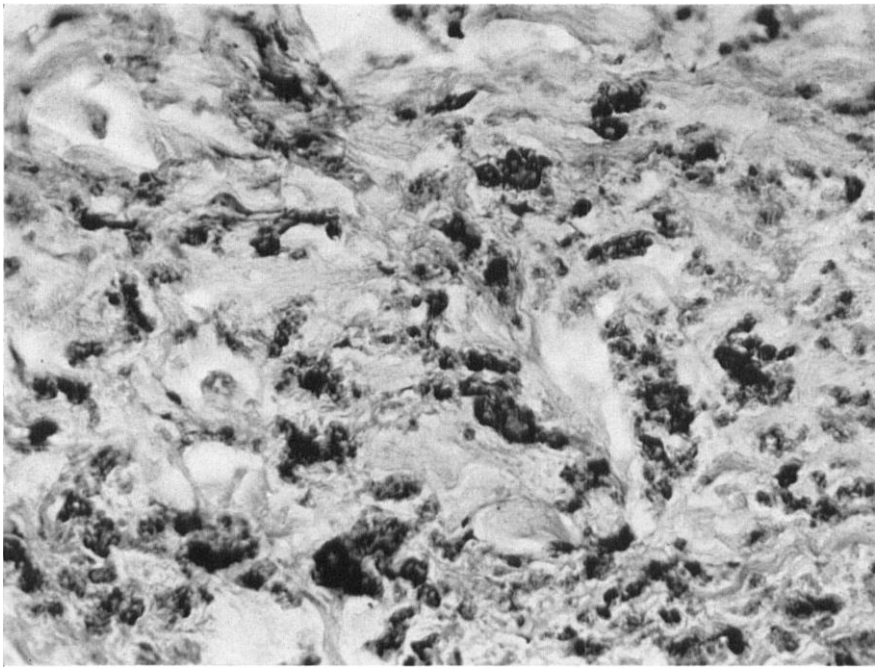

FIG. 7. Pseudoxanthoma elasticum. Toluidine blue stain. × 250. (Black-white picture × 385). Dark blue stained coarse elastic curls on a light stained collagen background.

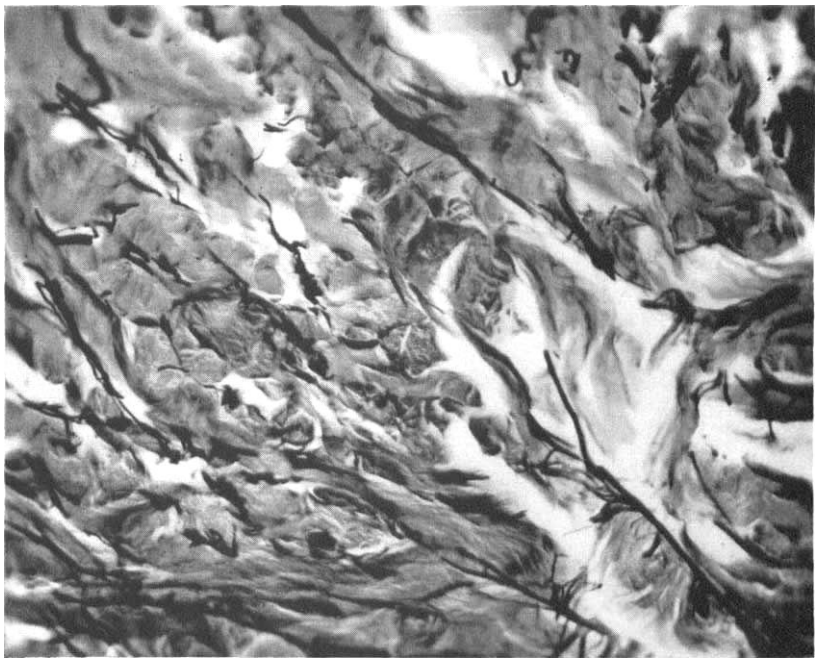

FIG. 8. Connective tissue nevus. Wilder's reticulum stain. × 265. Long, rather straight, and short, thick, dark, silver impregnated fibers; grayish staining of swollen collagen bundles.

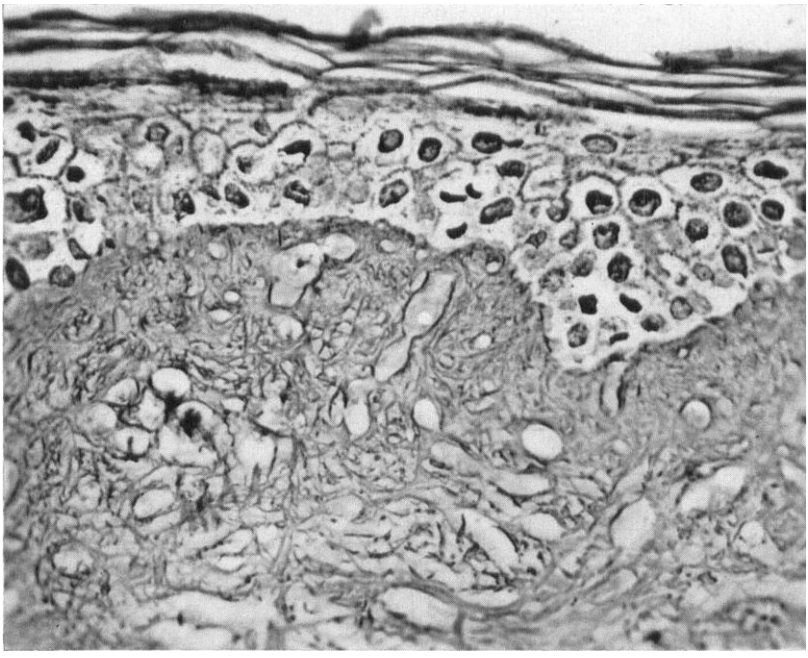

FIG. 9. Generalized scleroderma. Wilder's reticulum stain. × 540. Degeneration of reticulum. Fine argyrophilic shreds in basal membrane, subepidermally, and in the vascular walls.

There is no fibrinoid in the dermal connective tissue of collagen diseases. In scleroderma and scleredema the papillary and subepidermal fibers appear very fine and diffusely condensed. There is swelling and coarsening of collagen bundles in the connective tissue nevus (fig. 5). In Ehlers-Danlos' syndrome there is some reduction and irregularity of the connective tissue, and in pseudoxanthoma elasticum the collagen of the pars reticularis cutis is slightly fragmented.

The elastic tissue is usually well preserved in those lesions which contain little reticulum. The fine elastica of the papillae in Ehlers-Danlos' syndrome seems somewhat increased and more ramified. The elastic tissue appears normal in chronic lymphedema. The amount of elastic tissue in pseudoxanthoma elasticum is increased rather than decreased, although the characteristic elastic curls are coarse and irregular. In the upper cutis of the connective tissue nevus there is a reduction of elastic fibers. In scleroderma, scleredema, lupus erythematosus and granuloma annulare, in this sequence, the elastica shows progressive degeneration and atrophy, but even in lupus erythematosus there are still sometimes considerable numbers of elastic fibers present. In chronic radiodermatitis, however, the elastic tissue is virtually completely atrophic.

COMMENTS

The only large masses of PAS-positive connective tissue fibers in the examined degenerative and congenital dermatoses are the basophilic degenerations in light-exposed areas of chronic lupus erythematosus and in chronic radiodermatitis (15, 36, 41, 50, 59; also cf. Part A). These bundle conglomerates, therefore, are not characteristic for the named diseases, except in those cases where they are found in areas of non-exposed skin.

Otherwise, in contrast to tumorous and infiltrative lesions (48) very little of mucopolysaccharides is revealed by histochemical stains in degenerative and dysplastic cutaneous lesions. In collagen diseases the normally PAS-positive dermal structures, i. e., basal membranes and vascular walls (3, 6, 31, 40, 50) are more heavily outlined by PAS. This was already noticed by previous authors 5, 50).

In scleroderma, scleredema and Ehlers-Danlos' syndrome there is moderate, diffuse PAS-fuchsinophilia and toluidine blue metachromasia of the subepidermal layer.

PAS-positive fibers which are also argyrophilic and morphologically atypical occur in chronic radiodermatitis, granuloma annulare and connective tissue nevus. The same peculiar fibers were observed also in the stroma of cutaneous tumors and granulations (48). There is no other fuchsinophilic collagen in cutaneous degenerations and dysplasias. The reticulum fibers stain red with PAS, as usual (31, 35). Undoubtedly, part of the staining of basal membranes *and* vascular walls in the lesions of "collagen diseases" is due to the presence of reticulum fibers (6, 27, 34, 50).

On the other hand, in many degenerative and dysplastic lesions the reticulum fibers fail to stain with PAS. A morphologically and tinctorially normal reticulum

is only present in chronic radiodermatitis and granuloma annulare. Degeneration of reticulum, also observed by previous workers (6, 38, 39, 48, 56) is demonstrable, particularly with silver stains in collagen diseases. Degenerative reticulum loses its PAS-fuchsinophilia. As described in a previous report (48), this was noticed likewise in the reticulum of the stroma of certain cutaneous granulomas and lymphoblastomas. The lack of new formation of collagen is probably a consequence of the degeneration of reticulum fibers (2, 13, 31, 38; cf. also Part A).

The reduced PAS staining of reticulum and, in particular, the virtual absence of PAS-positive collagen account for the scantiness of histochemically demonstrable mucopolysaccharides in degenerative and dysplastic cutaneous lesions in comparison with the amounts encountered in connective tissue tumors or senile degeneration of the skin (48 and Part A). Another reason is the lack of metachromatic and PAS-positive fibrinoid in the cutaneous lesions of collagen diseases whereas its presence is characteristic of the connective tissue changes in visceral lesions (7, 21, 22). There is, at most, a slight amount of fibrinoid in the vascular walls. Incidentally, this and all other PAS-positive substances in degenerations and dysplasias are mucoproteins since they stain beta metachromatic and are hyaluronidase-stable (31, 35, 40).

Fiber changes seem much more conspicuous in cutaneous degenerations and dysplasias than changes of the ground substance (1). Ehlers-Danlos' syndrome, e. g., also was recently attributed to faulty intertwining of fibers (18). The collagen bundles of the connective tissue nevus show swelling, and they contain rare PAS-positive, argyrophilic fibers. Orceinophilic collagen was also observed in this lesion (42). In pseudoxanthoma elasticum there is some fragmentation of collagen fibers.

Elastic atrophy has been described by many observers (1, 15, 36, 39, 41, 59). In congenital dysplasias there is damage to the elastic tissue not only in pseudoxanthoma elasticum but also in the connective tissue nevus (49), and an increase in elastic fibers seems to be present in Ehlers-Danlos' syndrome (19, 52).

In some discrepancy with the histologic findings, the collagen fibers of lupus erythematosus and scleroderma appear essentially undamaged under the electron microscope (4, 13, 47, 52). In Ehlers-Danlos' syndrome their number is greatly reduced; in pseudoxanthoma elasticum, on the contrary, they are abundant (52).

These electron-microscopic findings, of course, throw doubt on the role of fiber degeneration in collagen diseases. On the other hand, changes of the cutaneous ground substance also seem insignificant in these diseases. Thus, the basic pathology of the cutaneous tissue in degenerative and dysplastic conditions appears even more obscure than ever before. The explanation perhaps lies in quantitative changes of the ground substance which histochemically are not demonstrable. Meyer (35) pointed to a quantitative aspect in the histochemical staining of mucopolysaccharides, and Musso (39) and Seville (47) could actually demonstrate, by trypsin digestion of scleroderma tissue, and electron-microscopically, that in that disease there is an increased amount of normal, i. e., histochemically unstained, ground substance in the tissue.

SUMMARY

1. The basophilic connective tissue of exposed skin is PAS-positive, beta-metachromatic and slightly hyaluronidase-labile. It represents a conglomeration of mucoproteins and free acid mucopolysaccharides of the ground substance with abnormal cutaneous fiber masses.

2. These fiber masses consist of morphologically and tinctorially *abnormal collagen as well as elastic and reticulum fibers.*

3. *The absence of a repair process in the areas of basophilic degeneration is probably due to the abnormal state of the reticulum.*

4. In extremely advanced basophilic degeneration the fibrous structure of the conglomerates is lost, the tissue becomes amorphous, and the staining reactions of the mucoid substances are decreased.

5. Degenerative cutaneous lesions, or more specifically processes pertaining to the "collagen diseases", and congenital dysplasias, histochemically show only small amounts of mucopolysaccharides.

6. Nevertheless, the basement membranes and vascular walls in lupus erythematosus, scleroderma, scleredema and chronic radiodermatitis show PAS staining of increased intensity. There is moderate, diffuse PAS staining of the papillae and subepidermal zones in scleroderma, and Ehler-Danlos' syndrome. The reticulum fibers of chronic radiodermatitis and granuloma annulare are distinctly PAS-positive.

7. Most PAS-fuchsinophilic structures show beta metachromasia with toluidine blue. This metachromasia is hyaluronidase-stable which indicates the presence of mucoproteins.

8. Except in chronic radiodermatitis and granuloma annulare the argyrophilic fibers show degenerative changes or atrophy. The degenerative reticulum is usually PAS-negative.

9. Only small amounts of mucoid substances being demonstrable in degenerative and dysplastic conditions of the skin, the basic pathology of these conditions may involve quantitative changes of the ground substance and/or its components, which cannot be demonstrated histochemically.

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